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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/631,351	07/31/2003	Oliver Harnack	450117-04465	3470
7590 01/04/2006 FROMMER LAWRENCE & HAUG LLP 745 FIFTH AVENUE NEW YORK, NY 10151			EXAMINER YU, MELANIE J	
			ART UNIT 1641	PAPER NUMBER

DATE MAILED: 01/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/631,351

Applicant(s)

HARNACK ET AL.

Examiner

Melanie Yu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 August 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 1 and 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

1. Applicant's amendments and arguments filed 1 August 2005 has been entered. Claims 2, 5 and 21 are currently amended. Claims 22 and 23 are canceled. Claims 1 and 21 are withdrawn. Claims 1-21 are currently pending in this application.

#### ***Election/Restrictions***

2. Examiner restricted the claims into three groups, claims 1 and 3-20, claims 2-20 and claim 21. Applicant argues that examiner has articulated reasons why the inventions are independent or distinct, but has not discussed as to why having independent and distinct inventions within the same application presents a serious burden on the examiner. The inventions of the groups listed above present a serious burden on the examiner because they require different search strategy. The group of claims 1 and 3-20 requires a search for exposing hydrophilic macromolecules to hydrophilic species and then immobilizing the combination on a hydrophobic surface, which is different from the search for the method of claims 2-20 which would require a search for immobilizing a hydrophilic macromolecule on a hydrophobic surface and then exposing a hydrophilic species to the immobilized hydrophobic macromolecule. Claim 21 is a nanoassembly that can be made by either of the methods of claims 1 or 2, and therefore a search for the nanoassembly would not necessarily encompass a search for either of the methods of claims 1 or 2. Furthermore, a search for the method of claim 1 would not encompass a search for the method of claim 2, because the two methods cannot coexist. Therefore, in the case of the instant application, it would be a serious search burden on the examiner to examine more than one of the independent or distinct inventions.

***Claim Objections***

1. Claims 3-20 objected to because of the following informalities: The claims depend from non-elected claim 1. Appropriate correction is required.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 2-18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Caldwell et al. (US 5,516,703).

Regarding claims 2, 3 and 14-18 Ford et al. teach a method of attaching a hydrophilic species to hydrophilic macromolecules immobilized on a surface, comprising the steps: providing a surface (par. 0019; par. 0078; par. 0082); immobilizing hydrophilic nucleic acids (hydrophilic macromolecules) on the surface (par. 0019; par. 0078; par. 0082); and exposing the nucleic acids immobilized on the surface to metal complexes (par. 0079) of gold nanoparticles (a hydrophilic species, par. 0010), whereby the hydrophilic species are attached to the hydrophilic macromolecules (metallization of DNA shows metal particle attachment of DNA, par. 0079), and wherein the nucleic acid is DNA (par. 0020) and is double-stranded or single-stranded (par. 0020). Ford et al. fail to teach the surface being hydrophobic.

Caldwell et al. teach a hydrophobic substrate (col. 7, lines 19-30), in order to provide a surface with specific reactivity.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Ford et al., a hydrophobic surface as taught

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by Caldwell et al., in order to provide a surface with a high degree of reactivity and little or no background non-specific reactivity.

With respect to claims 4 and 11, Ford et al. teach the hydrophilic species in a water solution (par. 0023).

Regarding claims 5, 6 and 20, Ford et al. teach an additional step of growing an attached hydrophilic species to a larger size and wherein the attached hydrophilic species is exposed to an electroless plating solution (enlargement of particles by electroless deposition, par. 0010). Ford et al. further teach the electroless plating solution (par. 0011; par. 0030) comprising a gold salt and a reducing agent (solution contains metal ion species of Au and reducing reagent, par. 0011).

With respect to claims 7-10, Ford et al. teach immobilizing the hydrophilic macromolecules on the surface by applying the hydrophilic macromolecules to the surface (par. 0078) by spin-coating (par. 0078). Ford et al. further teach exposing the hydrophilic macromolecules to the species for 10 minutes (par. 0079), which is encompassed by the recited ranges of between 1 second and 20 minutes and between 10 seconds and 10 minutes. Wherein the surface is hydrophobic as taught by Caldwell et al.

Regarding claims 12 and 13, Caldwell et al teach a water contact angle of greater than about 60° (col. 7, lines 18-30), which encompasses the recited ranges of from 30° to 110° and 60° to 110°.

3. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Caldwell et al. (US 5,516,703) as applied to claim 2, further in view of Berning et al. (<sup>198</sup>Au-Labeled Hydroxymethyl Phosphines as Models for Potential Therapeutic Pharmaceuticals, 1998, Nuclear Medicine & Biology, Vol. 25, pages 577-583).

Ford et al. in view of Caldwell et al., as applied to claim 2, teach a method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface, but fail to teach the hydrophilic species being tris(hydroxymethyl)phosphine-gold nanoparticles.

Berning et al. teach a hydrophilic species of tris(hydroxymethyl)phosphine-gold nanoparticles (581, Discussion, 1<sup>st</sup> paragraph), in order to evaluate their potential utility in the design of Au(I)-containing drugs.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Ford et al. in view of Caldwell et al., a tris(hydroxymethyl)phosphine-gold nanoparticle as taught by Berning et al., in order to provide metal complexes that exhibit *in vitro* stability.

#### ***Double Patenting***

4. Claims 2-6, 11, 15 and 17-19 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 14 and 15 of copending Application No. 10/210812 in view of Caldwell et al. (US 5,516,703). Claims 1 and 2 of application '812 recite a hydrophilic macromolecule (nucleic acid) exposed to a hydrophilic nanospecies (tris(hydroxymethyl)phosphine-Au) and the complex immobilized on a substrate. However, application '812 fails to recite a hydrophobic substrate. Caldwell et al. teach immobilization on a hydrophobic substrate to prevent non-specific binding. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of application '812, a hydrophobic substrate as taught by Caldwell et al., in order to prevent non-specific binding of hydrophilic nanospecies to the substrate. Claims 3, 4, 5, 14 and 15 of application '812 recite a hydrophilic species in a water solution, the species

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grown to a larger size with an electroless plating solution, and the metal for the nanospecies being Au. Claim 4 recites the nucleic acid being single or double stranded.

5. Claims 2-6, 11, 15 and 17-19 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 14-16 and 20 of copending Application No. 09/990,049 in view of Caldwell et al. (US 5,516,703). Claims 1, 2 and 16 of application '049 recite a hydrophilic macromolecule (nucleic acid) exposed to a hydrophilic nanospecies (metal complex) and the complex immobilized on a substrate. However, application '049 fails to recite a hydrophobic substrate. Caldwell et al. teach immobilization on a hydrophobic substrate to prevent non-specific binding. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of application '049, a hydrophobic substrate as taught by Caldwell et al., in order to prevent non-specific binding of hydrophilic nanospecies to the substrate. Claims 2-4, 14-16 and 20 of application '049 recite a hydrophilic species in a water solution, the species grown to a larger size with an electroless plating solution, and the metal for the nanospecies being Au. Claim 4 recites the nucleic acid being single or double stranded.

This is a provisional obviousness-type double patenting rejection.

### ***Response to Arguments***

6. Applicant's arguments filed 1 August 2005 have been fully considered but they are not persuasive.

7. Regarding the rejection of claims 2-18 and 20 under 35 USC 103(a) over Ford in view of Caldwell, applicant argues that the examiner does not explain why it would have been obvious to one having ordinary skill in the art to select one isolated element from Caldwell's invention for

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substitution into Ford. However, examiner relies upon the substrate of Caldwell to provide non-specific binding and low background activity, which would provide the method of Ford with a substrate comprising components for advantageous immobilization. Applicant argues that the motivation comes from examiner's opinion and not from any factual support from Ford or Caldwell. However, Caldwell specifically states that the hydrophobic substrate, which includes a polymeric coating, is beneficial by providing a non-specific binding surface with reduced background signal at column 2, lines 32-36 and column 3, lines 30-36.

Applicant argues that a prior art reference must be considered in its entirety include portions that would lead away from the claimed invention. Applicant also argues that it is impermissible to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art. However, Caldwell does not teach away from using the hydrophobic substrate coated with a polymer in the method of Ford and examiner does not exclude parts that teach away from using the substrate of Caldwell in the method of Ford.

Applicant argues that Caldwell fails to teach a hydrophobic substrate and instead teach a modified polymeric surfactant adsorbed upon a hydrophobic polymer substrate which renders a hydrophilic substrate and the substrate is therefore not hydrophobic. However, the substrate coated with the polymer is still hydrophobic, and the polymeric layer is considered to be part of the hydrophobic substrate. It would have been obvious to one having ordinary skill in the art to substitute the entire hydrophobic substrate of Caldwell, which comprises the hydrophilic polymer layer as pointed out by applicant, for the substrate of Ford in order to provide the



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advantage of non-specific binding and low background signal. Furthermore, claim 2 uses open claim language “comprising” which does not exclude a hydrophilic polymer layer coating the hydrophobic substrate to provide further advantages for immobilization of hydrophilic macromolecules. It is also noted that in the instant specification, at page 9, a step 2 is disclosed wherein a polymer film is formed on the hydrophobic substrate before immobilization of DNA.

Applicant argues the Berning reference is also used for an isolated element from within its teachings without considering the reference as a whole and examiner’s motivation for combination comes from the examiner’s opinion and not from any factual support. However, Berning specifically teaches that the tris(hydroxymethyl)phosphine-gold nanoparticles have increased stability at page 579, right column, Results section.

For the reasons stated above, Caldwell teaches a hydrophobic substrate comprising a polymeric layer, and therefore based on this argument the double-patenting rejection has not been overcome.

### ***Conclusion***

No claims are allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melanie Yu whose telephone number is (571) 272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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12/23/05